REMARKS

Claim 15 has been amended to more distinctly claim Applicants' invention. Support for the new amendment is found, for example, at page 7, lines 26-28 of the specification. Claims 22-23 have been added. Support for these new claims can be found at, for example, page 6, lines 4-9 of the specification. No new matter is added by the amendments, and entry is respectfully requested. Claims 15-23 are pending in the application. Reconsideration of the claims in view of the amendment and the following remarks is requested.

Drawings

The Examiner noted that the draftsperson has objected to the drawings. Applicants will submit new drawings within the time period set in the Office Action.

Specification

The Examiner objected to the title of the invention, stating that it is not descriptive. Applicants have amended the title to be more descriptive of the invention to which the claims are directed. Withdrawal of this objection is requested.

Claim objections

The Examiner objected to the numbering of the sub parts of claim 15. Applicants have amended claim 15 according to the Examiner's suggestions. Withdrawal of this objection is requested.

35 U.S.C. § 103(a)

Claims 15-21 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Huland in view of Debs and Ruskewicz. The Examiner states that Huland teaches aerosol compositions having cytokines combined with mannitol and polysorbates in concentrations within the scope of the claims. The Examiner concluded that it would have been obvious to generate a composition containing mannitol and polysorbate with a specific viscosity as described by Huland and using the extrusion mechanism of Ruskewicz.

Applicants respectfully traverse this rejection. Claim 15 as amended recites a liquid-droplet aerosol composition comprising a stabilizing agent consisting of sugar, alcohol, amino acid, or a combination thereof. Applicants submit that neither Huland, Ruskewicz, nor Deb disclose a gamma interferon composition comprising a stabilizing agent consisting of sugar, alcohol, amino acid, or a combination thereof.

Rather, Huland teaches an aerosol comprising a serum protein, and preferably human serum albumin, as a stabilizing agent (column 5, lines 23-27). The purpose of the serum protein is to optimize the biological effect of the cytokine, and to lead to a better recovery after in vitro nebulization (lines 24-27). Huland discloses that serum protein concentrations of between 0.1-20% by weight of the aerosol correlated in a dose-dependent manner with the level of recovery of the cytokine after nebulization (column 5, lines 35-37). Furthermore, Huland teaches that only at very high levels of cytokine (at least 0.5 mg/ml) can the serum protein be omitted while still allowing recovery and biological activity of the drug (column 5, lines 37-39).

Claim 15 of the present invention, in contrast, recites an aerosol composition wherein the biological activity of the aerosolized gamma interferon is substantially the same as that of the solution.

Neither Deb nor Ruskewicz remedy this deficiency of Huland. Applicants respectfully submit, therefore, that none of the cited references (Huland, Deb, and Ruskewicz), alone or in combination, teach or suggest a composition having all the limitations of claim 15, at least for this reason. Applicants submit, therefore, that claim 15 is patentable over Huland in view of Deb and Ruskewicz. Since each of claims 16-21 depend from, and add additional limitations to, claim 15, Applicants submit that these claims are also patentable over these references. Withdrawal of the rejection is respectfully requested.

Furthermore, the independent claims presently recite that the droplets have a narrow distribution of sizes that is less than 2 standard deviations from the volume mean diameter of the droplets, (claim 15), or a narrow particle distribution such that at least 80% of the droplets have a diameter in a selected size range (claim 22). It can be helpful for particles making up an aerosol composition to have a narrow particle distribution (page 6, lines 4-9 of the specification). The ability to regulate the particle size distribution of the aerosol can help allow the targeting of the aerosol to a desired location, e.g., to bronchial sites, other areas of the respiratory tract, or systemically (page 15, lines 1-7). It is a feature of the claims, therefore, that the composition can form aerosol liquid droplets within a well-defined size range or size ranges (page 7, lines 3-4). The invention discloses a combination of novel composition and aerosolization conditions that have been found to achieve these goals (page 7, lines 6-8).

Applicants respectfully submit that none of Huland, Deb, or Ruskewicz, alone or in combination, teach or suggest a γ-IFN aerosol having a narrow particle distribution as recited in the present claims. Applicants submit, therefore, that the claims are patentable over these references for this additional reason.

Finally, the independent claims each recite that the biological activity and molecular size distribution of the γ-IFN in the aerosol is substantially the same as that of the aqueous γ-IFN solution used to form the aerosol. Before the present invention, it was not known that γ-IFN could be formulated so that its activity and molecular-size characteristics are maintained over an extended storage condition, yet still allow the desired protein properties and particle-size features in an aerosol (page 2, lines 11-14 of the specification). This uncertainty may be partly caused by the fact that γ-IFN is active in a non-covalent dimeric form, but not in monomeric form (page 2, lines 9-10). γ-IFN aerosolization can lead to loss of activity and/or protein aggregation, particularly where the aerosol is formed under shear conditions necessary to produce a desired aerosol-particle range (page 2, lines 5-9).

Applicants submit that the Huland reference does not teach or suggest that a γ-IFN solution can be aerosolized while substantially maintaining a biological activity and molecular size distribution of the γ-IFN in the aerosol relative to that of the aqueous γ-IFN solution used to form the aerosol. Neither Deb nor Ruskewicz remedy this deficiency. Therefore, the claims are patentable over these references for this additional reason.

Conclusion

Applicants submit that all claims are in condition for allowance. Notice of such allowance is requested. The Examiner is invited to telephone the undersigned attorney for clarification of any of the amendments and remarks or to otherwise speed prosecution of this application.

Respectfully submitted,

MERCHANT & GOULD, P.C.
P.O. Box 2903
Minneapolis, Minnesota 55402-0903
(612) 332-5300

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By: Garen Gotfredson

Garen J. Gotfredson
Reg. No. 44,722